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Clinical and anamnestic characteristics of patients depending on left ventricular ejection fraction: results of a register study

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ABSTRACT

Aim. To study the clinical and anamnestic features of patients followed up in the Center for Chronic Heart Failure at the Regional Vascular Center according to the data of the corresponding register.

Materials and methods. The study included data of 802 patients included in the Kuzbass Register of Patients Followed up at the Center for Chronic Heart Failure from 2020 to 2022. The median follow-up was 1.6 ± 0.7 years.

Results. According to the present register, men dominated in the gender profile of patients with chronic heart failure – 612 (76.3%) participants ($p < 0.001$). The largest group of subjects was represented by patients with a low left ventricular ejection fraction (less than 40%) – 546 people. This category was also characterized by a more severe functional class of chronic heart failure (New York Heart Association); patients with functional class III–IV chronic heart failure prevailed ($p < 0.001$).

The most common comorbidities revealed were chronic kidney disease (glomerular filtration rate of less than 60 ml / min / 1.73 m² according to the CKD-EPI equation) – 614 (76.5%) patients and obesity (body mass index of more than 30 kg / m²) – 334 (41.6%) patients. Type 2 diabetes mellitus was reported in 193 (24%) patients. The analysis of the etiology of chronic heart failure showed that the main causes of heart failure in the groups with low and intermediate left ventricular ejection fraction were coronary heart disease and combined causes, whereas in the group with preserved left ventricular ejection fraction, the disease resulted from coronary heart disease and arrhythmogenic causes.

Conclusion. Assessing the clinical and anamnestic features of patients with heart failure, it can be said that these people are mainly male, retired, with coronary heart disease, low left ventricular ejection fraction, and a comorbidity, mainly chronic kidney disease, diabetes mellitus, and obesity.

Keywords: chronic heart failure, coronary heart disease, cardiology, left ventricular ejection fraction

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Клинико-анамнестические особенности пациентов в зависимости от величины фракции выброса левого желудочка: результаты регистрового исследования

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РЕЗЮМЕ

Цель. Изучить клинико-анамнестические особенности пациентов, наблюдающихся в центре хронической сердечной недостаточности на базе регионального сосудистого центра по данным соответствующего регистра.

Материалы и методы. В настоящее исследование вошли данные 802 пациентов из Кузбасского регистра пациентов, наблюдающихся в центре помощи больным с хронической сердечной недостаточностью, включенных за период с 2020 по 2022 г. Средний срок наблюдения составил $1,6 \pm 0,7$ лет.

Результаты. По данным настоящего регистра, в гендерной структуре пациентов с хронической сердечной недостаточностью преобладали мужчины – 612 (76,3%) ($p < 0,001$). Наибольшую группу исследуемых составляли пациенты с низкой фракцией выброса левого желудочка (менее 40%) – 546 человек. Данная категория была и более тяжелой по функциональному классу хронической сердечной недостаточности (New York Heart Association), преобладали больные с функциональным классом III–IV ($p < 0,001$).

При анализе коморбидной патологии выявлено, что наиболее распространенными являлись: хроническая болезнь почек (скорость клубочковой фильтрации по СКД-EPI менее 60 мл/мин/1,73 м²) – 614 (76,5%) человек и ожирение (индекс массы тела более 30 кг/м²) – 334 (41,6%) пациента. Сахарный диабет 2-го типа был зарегистрирован у 193 (24%) пациентов. Анализ этиологии хронической сердечной недостаточности показал, что основными причинами сердечной недостаточности в группах низкой и промежуточной фракций выброса являлись ишемическая болезнь сердца и комбинированные причины, в группе с сохранной фракцией выброса – ишемическая болезнь сердца и аритмогенная причины.

Заключение. Таким образом, оценивая клинико-анамнестические особенности пациентов с сердечной недостаточностью, можно говорить о том, что это лица преимущественно мужского пола, пенсионного возраста, с ишемической болезнью сердца и низкой фракцией выброса левого желудочка, а также имеющие коморбидную патологию, преимущественно хроническую болезнь почек, сахарный диабет и ожирение.

Ключевые слова: хроническая сердечная недостаточность, ишемическая болезнь сердца, кардиология, фракция выброса левого желудочка

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

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INTRODUCTION

Reducing mortality in chronic heart failure (CHF) among the population currently remains one of the most important and relevant issues in cardiology and healthcare in general. Patients with CHF are

characterized by a progressive course of the disease, which ultimately leads to multiple hospitalizations due to decompensation of CHF, prolonged medical and expensive surgical treatment, and high levels of disability and mortality [1]. According to various estimates, the prevalence of CHF is approximately

1–2% in the general population, and it steadily increases, reaching more than 10% among people over 70 years of age [2].

Considering the growing number of elderly people and the progressive growth of cardiovascular pathology, the prevalence of CHF is also increasing annually [3]. In this regard, a global strategic task is to find ways to detect CHF at earlier stages of the disease, including by understanding the clinical and anamnestic characteristics of patients with CHF [4]. To resolve this issue, an epidemiological study EPOCHA-CHF was conducted from 2002 to 2017 in the European part of Russia. Its findings made it possible to estimate the prevalence and mortality rate of CHF and create a clinical portrait of a patient with CHF [5].

In the course of evolution of knowledge about the pathophysiology of CHF, it has been proven that CHF can develop not only with reduced, but also with normal left ventricular ejection fraction (LVEF). According to the EPOCHA-CHF project in Russia, 71% of patients with CHF had LVEF of more than 60% [6]. An important goal of register studies is to create effective methods for monitoring the outpatient stage of treatment, drug therapy, and physical and psychological rehabilitation of patients, that are impossible without knowledge about the characteristics of the patient cohort. In recent years, CHF centers have been established in outpatient settings, which proved their effectiveness in reducing the risk of overall and cardiovascular mortality and decreasing the number of re-hospitalizations [7]. In the meantime, the effectiveness of this approach to management of patients with CHF requires additional study, including research from the standpoint of different CHF phenotypes.

The aim of the study was to investigate the clinical and anamnestic features of patients followed up in the CHF center at the Regional Vascular Center according to the data of the corresponding register, depending on the CHF phenotype.

MATERIALS AND METHODS

The study included data from the Kuzbass Register of Patients Followed up at the Center for Chronic Heart Failure. The register includes data of patients with heart failure after discharge from Kuzbass Clinical Cardiology Center named after L.S. Barbarash or patients with newly diagnosed heart failure in the outpatient or inpatient setting registered in the CHF center database. The register was launched on

26.08.2020. The register was managed in accordance with the provisions of the Declaration of Helsinki and was approved by the local Ethics Committee. All patients signed an informed consent to be followed up at the CHF center.

The register was a database which served as the basis for a prospective, cohort, observational study of adult patients. The only inclusion criterion for patients was to be followed up at the CHF center at the Kuzbass Clinical Cardiology Center named after L.S. Barbarash. When maintaining the register, all requirements of the Federal Law of 27.07.2006 No. 152-FZ “On Personal Data” were met. During the analysis, all patient data were marked and anonymized.

Clinical data were recorded in a specially designed patented electronic form when entered in the register and then at regular intervals during follow-up from medical and outpatient records. Basic information about patients included demographic data, social status, history of the underlying disease, concomitant diseases, vital signs, clinical, instrumental and laboratory parameters, doses of cardiovascular drugs, and follow-up diaries. Baseline socio-demographic data were self-reported by patients. For newly enrolled patients, monthly follow-up checkpoints took place during the first 3 months. They involved telephone calls by a nurse who filled out follow-up diaries and, if necessary, in-person visits to the CHF center with an examination by a cardiologist. Then examinations were carried out every trimester.

The study included data of 802 patients included in the Kuzbass Register of Patients Followed up at the CHF Center from 2020 to 2022. The median follow-up was 1.6 ± 0.7 years.

Statistical analysis was carried out using the Statistica 10.0 (Statsoft, USA) and SPSS 11 software packages. Normality of distribution was assessed using the Kolmogorov – Smirnov test. Quantitative variables were presented as the mean and the standard deviation $M \pm \sigma$. Continuous variables with normal distribution were compared using the Student’s *t*-test. To compare continuous variables with non-normal distribution, the nonparametric Mann – Whitney *U*-test was used. To compare three or more quantitative variables, the rank-based Kruskal – Wallis *H*-test was applied, followed by a pairwise comparison of groups using the Mann – Whitney test with the Bonferroni correction to estimate the *p* value. Discrete variables were compared using the χ^2 test with the Yates’ continuity correction. If one of the compared groups was small, the two-tailed Fisher’s test (*F* test) was

used. The differences were considered statistically significant at two-tailed $p < 0.05$.

RESULTS

According to the register, men prevailed in the gender profile of patients with CHF – 612 (76.3%) men, 190 women (23.7%), $p < 0.001$. The average age of the participants was 63.5 ± 11.2 years; men were younger than women: 62 ± 10.9 years and 67.5 ± 11.8 years, respectively, $p < 0.05$. The analysis of the place of residence showed that 626 (78.1%) patients were urban residents, and 176 (21.9%) participants were rural residents. The distribution of patients with a confirmed diagnosis of CHF by gender and age is shown in Figure 1.

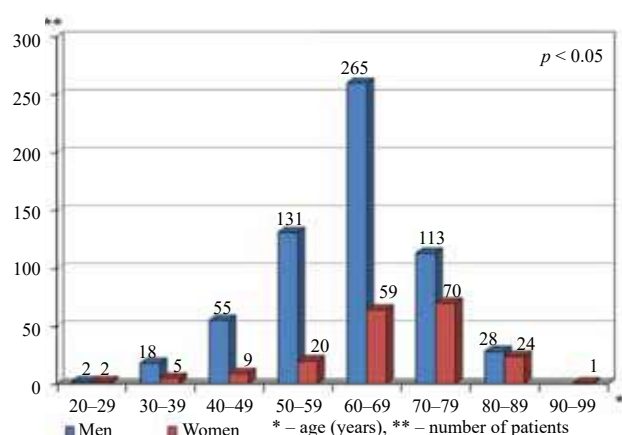


Fig. 1. Gender and age characteristics of patients with CHF

According to echocardiography findings, the average LVEF measured by the Simpson method was $37 \pm 15.4\%$ in the general sample. Patients with LVEF $< 40\%$ prevailed (Fig. 2).

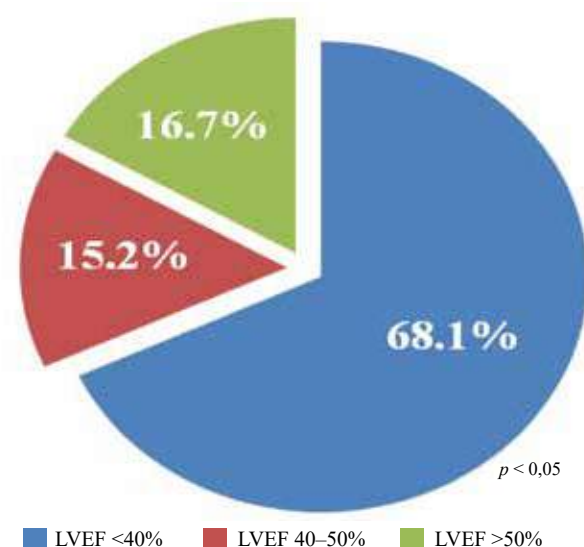


Fig. 2. Distribution of patients depending on LVEF: HFrEF – heart failure with reduced ejection fraction, HFmEF – heart failure with midrange ejection fraction, HFpEF – heart failure with preserved ejection fraction, n – number of patients, p – statistical significance

Distribution of the patients by stages and severity of CHF (NYHA functional class) depending on LVEF is presented in Table 1. The largest group was represented by patients with reduced LVEF (less than 40%) – 546 people. This category was also characterized by a more advanced functional class of CHF; patients with NYHA III–IV CHF prevailed, $p < 0.001$.

Peculiarities of gender distribution depending on the HF phenotype were identified. Thus, in the group with reduced LVEF, male patients prevailed; in the groups with midrange and preserved LVEF, there were more women.

Table 1

Stages and NYHA functional class of chronic heart failure depending on the phenotype, n (%)				
Parameter	HFrEF ($< 40\%$), $n = 546$ (%)	HFmEF (40–49%), $n = 122$ (%)	HFpEF ($\geq 50\%$), $n = 134$ (%)	$\chi^2; p$
Stage by the Strazhesko – Vasilenko classification				
Stage I CHF	5 (0.9)	18 (14.7)	74 (55.2)	299.431; < 0.001
Stage IIA CHF	359 (65.8)	69 (56.5)	43 (32.1)	50.578; < 0.001
Stage IIB CHF	182 (33.3)	35 (28.7)	17 (12.7)	22.213; < 0.001
NYHA functional class				
NYHA I	–	–	5 (3.7)	25.082; < 0.001
NYHA II	59 (10.8)	33 (27.0)	106 (79.1)	270.366; < 0.001
NYHA III	379 (69.4)	39 (32.0)	19 (14.2)	161.800; < 0.001
NYHA IV	108 (19.8)	50 (41.0)	4 (3.0)	57.389; < 0.001

The analysis of comorbid pathology in the studied patients revealed that the most common were chronic kidney disease (CKD) (glomerular filtration rate of less than 60 ml / min / 1.73 m² according to the CKD-EPI equation) – 614 (76.5%) patients and obesity (body mass index of more than 30 kg / m²) – 334 (41.6%) patients. Type 2 diabetes mellitus was reported in 193 (24%) patients.

The analysis of the dependence of comorbidity on the CHF phenotype showed that in patients with reduced LVEF, CKD predominated; as expected, such patients more often had an implantable cardioverter – defibrillator (ICD) implanted. In patients with preserved LVEF, diabetes and chronic obstructive pulmonary tuberculosis (COPD) were more common, and in the group with midrange LVEF – prior stroke and anemia (Table 2).

Table 2

Anamnestic factors in patients with CHF depending on the disease phenotype, <i>n</i> (%)				
Parameter	HFrEF (< 40%), <i>n</i> = 546 (%)	HFmEF (40–49%), <i>n</i> = 122 (%)	HFpEF (≥ 50%), <i>n</i> = 134 (%)	χ^2 ; <i>p</i>
Men	459 (84.0)	84 (68.8)	69 (51.5)	67.573; <0.001
Type 2 diabetes mellitus	112 (20.5)	39 (32.0)	42 (31.3)	8.806; 0.013
Obesity	223 (40.8)	62 (50.8)	49 (36.5)	5.792; 0.056
Prior stroke	74 (13.5)	31 (25.4)	24 (17.9)	10.783; 0.05
COPD	18 (3.3)	5 (4.1)	12 (8.9)	8.279; 0.016
CKD (≥Stage 3A)	482 (88.2)	60 (49.1)	72 (53.7)	131.652; <0.001
Anemia	42 (7.6)	31 (25.4)	10 (7.4)	35.183; <0.001
Implanted ICD	69 (12.6)	7 (5.7)	2 (1.5)	17.828; <0.001

The analysis of the etiology of CHF showed that more than half of the patients – 452 (56.3%) were diagnosed with coronary heart disease (CHD). It is worth noting that all patients with CHD in the study had arterial hypertension, and, therefore, these pathologies were considered together and did not belong to the “two or more causes” group. Among patients with CHD, 387 (85.6%) people suffered myocardial infarction, and 65 (14.4%) people were diagnosed with ischemic cardiomyopathy. Only in 4 (0.5%) patients, the cause of CHF development was isolated hypertension. Dilated cardiomyopathy (DCM) was the cause of CHF in 70 (8.7%) patients, atrial fibrillation or flutter – in 36 (4.5%) patients, previous myocarditis – in 13 (1.6%) cases, valvular defects – in 8 (1.0%)

patients. In almost every fourth patient (219 (27.4%) cases), the cause of CHF was a combination of two or more pathologies, while coexisting CHD (angina and / or post-infarction cardiosclerosis) and persistent or permanent forms of atrial fibrillation were the most common comorbidities in 182 (83.1%) patients.

The analysis of the etiology of CHF depending on the disease phenotype showed that the main causes of heart failure in the groups with reduced and midrange LVEF were CHD and combined causes, while in the group with preserved LVEF, CHF mostly resulted from CHD and arrhythmogenic causes.

Changes in the drug therapy received by the patients prior to and during the follow-up at the CHF center are presented in Table 4.

Table 3

Etiology of CHF depending on the disease phenotype, <i>n</i> (%)				
Parameter	HFrEF (< 40%), <i>n</i> = 546 (%)	HFmEF (40–49%), <i>n</i> = 122 (%)	HFpEF (≥ 50%), <i>n</i> = 134 (%)	χ^2 ; <i>p</i>
CHD	315 (57.7)	44 (36.1)	93 (69.4)	30.092; <0.001
PICS, <i>n</i> (%) – from CHD)	297 (94.3)	37 (84.1)	53 (57.0)	28.012; <0.001
ICM, <i>n</i> (%) – from CHD)	18 (5.7)	7 (15.9)	40 (43.0)	102.946; <0.001
Arrhythmogenic	17 (3.1)	5 (4.1)	14 (10.4)	13.550; 0.002
DCM	39 (7.1)	23 (18.9)	8 (6.0)	18.699; <0.001
Valvular defects	5 (0.9)	3 (2.5)	–	4.026; 0.134
Postmyocardial	7 (1.3)	4 (3.2)	2 (1.5)	2.510; 0.26
Hypertension	–	–	4 (3.0)	20.040; <0.001
Two and more causes	163 (29.9)	43 (35.2)	13 (9.7)	26.581; <0.001

Note. PICS – post-infarction cardiosclerosis, ICM – ischemic cardiomyopathy.

Table 4

Frequency of prescription of drug therapy, <i>n</i> (%)			
Parameter	Drug therapy prior to the follow-up at the CHF center, <i>n</i> = 802	Drug therapy during the follow-up at the CHF center, <i>n</i> = 802	χ^2 ; <i>p</i>
ACEI	459 (57.2)	573 (71.4)	35.313; <0.001
ARB	79 (9.8)	98 (12.2)	2.293; 0.130
ARNI	30 (3.7)	124 (15.4)	63.470; <0.001
BAB	652 (81.3)	706 (88.0)	14.001; <0.001
Statins	586 (73.1)	654 (81.5)	16.432; <0.001
MCRA	468 (58.4)	493 (61.4)	1.622; 0.203
Diuretics	540 (67.3)	681 (84.9)	68.191; <0.001
Antiarrhythmic drugs	139 (17.3)	172 (21.4)	4.344; 0.038
Antiplatelets	406 (50.6)	504 (62.8)	24.391; <0.001
OAC	117 (14.6)	166 (20.6)	10.302; 0.002
CCB	290 (36.2)	361 (45.0)	13.033; <0.001
SGLT2i	64 (7.9)	417 (52.0)	370.023; <0.001

Note. ACEI – angiotensin-converting enzyme inhibitor, ARB – angiotensin receptor blocker, ARNI – angiotensin receptor – neprilysin inhibitor, BAB – beta-adrenergic blocker, MCRA – mineralocorticoid receptor antagonist, OAC – oral anticoagulant, CCB – calcium channel blocker, SGLT2i – sodium – glucose cotransporter 2 inhibitors.

Prior to the follow-up at the CHF center, only 30% of patients were followed up by a cardiologist. No more than 46% of patients with HFrEF received optimal drug therapy, which involved the simultaneous use of renin – angiotensin – aldosterone system (RAAS) inhibitors, BAB, and MCRA. Only in 3% of cases, dose titration to the target dose was performed. As seen from Table 4, the follow-up at the CHF center led to increased adherence to therapy with RAAS inhibitors, SGLT2i, diuretics, antiarrhythmic drugs, and OAC. Still, an unsatisfactory number of patients adhered to optimal drug therapy.

DISCUSSION

The analysis of the data obtained revealed that men prevailed among patients with CHF, and the men / women ratio was almost 3:1. However, according to the results of the EPOCHA-Decompensation-CHF study, there were significantly more women participating in the study than men: 56.8 and 43.2%, respectively, $p = 0.001$ [6]. Therefore, the issue of gender distribution in CHF remains open. In a number of studies, researchers tried to answer the question of whether gender inequality was associated only with the prevalence of male patients or whether there were other reasons for this phenomenon [8–10]. It was noted that a smaller number of women may be due to the predominance of females in the cohort of patients with HFpEF, better subjective and clinical tolerability of CHF, and, therefore,

low demand for medical care and low detection of CHF [11].

The data obtained in the present study partially support this theory. Thus, in the group with HFrEF, men prevailed, and in the group with HFpEF, women predominated. The analysis of age-related characteristics, as expected, showed that the number of patients with CHF naturally increased with age, reaching a maximum in the age group of 60–69 years ($p < 0.05$). Further, after 69 years of age, a sharp decrease in the number of male patients was registered, which was associated with a natural population decline. For female patients, this trend was observed only starting from 80 years of age – due to longer life expectancy. Early incidence of CHF in men was explained by the manifestation of CHD as the main cause of CHF at a younger age compared to women [12]. Therefore, the data obtained once again emphasize the importance of measures for primary and secondary prevention of CHD, including from the standpoint of reducing CHF morbidity and mortality.

It is important that about 70% of patients with CHF are elderly – this category of patients is characterized by the presence of multiple comorbid pathologies, which significantly aggravates the course of CHF and may be a contraindication to modern high-tech treatment methods, such as implantation of devices and heart transplantation [13–15].

When analyzing the place of residence, it was shown that the vast majority of patients were urban residents.

The difference in the distribution of those studied between urban and rural residents was explained by lower availability of medical care for rural residents and the existence of only first aid stations in some territories. One way to solve this problem may be the on-site work of cardiology teams, which has already been implemented in Kuzbass.

The analysis of the distribution of CHF phenotypes showed that the predominant group, as expected, included patients with HFrEF, which corresponds to the data of other studies. Thus, according to various references, in the general population of patients with CHF, the prevalence of HFrEF is about 50% and HFmEF – 10–25% [16, 17]. Severe NYHA III–IV CHF is mainly characteristic of patients with HFrEF and HFmEF, while NYHA I–II CHF is more often detected in patients with HFpEF. The results show that identifying individuals with HFpEF remains a pressing issue. It is known that long-term HF without a clear clinical presentation and a lack of timely treatment may in the long term have a more significant negative impact on the prognosis than timely detected HFrEF [18–20].

CHD still remains the main cause of CHF, which is confirmed in the present study. It is largely due to previous myocardial infarction and ischemic cardiomyopathy that a group of patients with HFrEF is formed [21–23]. Almost always (100% according to the data of this study), CHD is accompanied by hypertension, whose contribution to the development of CHF should not be underestimated. Coexisting CHD and hypertension were the etiological cause of CHF in the majority of patients (56.3%), which is in line with the results of studies conducted in other countries. An epidemiological study conducted in the Republic of Belarus found that coexisting CHD and hypertension were the cause of CHF development in 65.5% of those studied [25]. The small number of studied patients in the hypertension group of CHF etiology may be explained by outpatient follow-up of these patients by internal medicine services, without follow-up at the CHF center.

Analyzing the features of drug treatment, the positive dynamics during the follow-up at the CHF center is worth noting. As the results show, one of the important advantages of such follow-up is increased compliance of prescribed therapy with existing clinical guidelines and patient adherence. Identification of patients with HFrEF who adhere to optimal drug therapy, based on registry data, makes it possible to optimize compilation of waiting lists for such types

of high-tech care as ICD implantation and orthotopic heart transplantation.

CONCLUSION

Assessing the clinical and anamnestic features of patients with heart failure followed up at the Kuzbass CHF center, it can be said that these people are mainly male, retired, with coronary heart disease, low left ventricular ejection fraction, and a comorbidity, mainly chronic kidney disease, diabetes mellitus, and obesity. This cohort of patients requires specific follow-up and management strategies aimed at increasing adherence, timely revascularization, social support, dynamic remote monitoring, and a multidisciplinary approach.

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